Intractable Epilepsy.

Sameh Morkous MD, FAAN
Lehigh Valley Health Network, sameh.morkous@lvhn.org

Published In/Presented At

Morkous, S. (2017, May). *Intractable Epilepsy*. Presentation Presented at: Lehigh Valley Epilepsy Education Exchange Spring Conference, Allentown, PA

Intractable Epilepsy

Is it still a sacred disease?

Sameh Morkous, MD, FAAN
Chief of Pediatric Neurology
Lehigh Valley Health Network
Allentown, PA

Lehigh Valley Health Network

Who We Are

- 8 Campuses
- 1 Children's Hospital
- 160+ Physician Practices
- 17 Community Clinics
- 16 Health Centers
- 12 ExpressCARE Locations
- 81 Testing and Imaging Locations
- 18,000+ Employees
- 2,005 Physicians
- 834 Advanced Practice Clinicians
- 4,208 Registered Nurses
- 57,272 Admissions
- 212,897 ED Visits
- 1,838 Acute Care Beds

Quality Milestones

2011

- **America's Best Hospitals for endocrinology, gastroenterology and geriatrics**-*U.S. News & World Report*
- **No. 1 and No. 2 Hospitals in the Region**-*U.S. News & World Report*
- **Magnet Hospital redesignation for nursing excellence**-*American Nursing Credentialing Center*
- **Top Performer on Key Quality Measures**-*Joint Commission*
- **Architecture and Design Award for environmentally friendly health care**-*GreenCare*
- **Top 100 Integrated Health Networks**-*Verispan*
- **100 Most Wired Hospitals**-*Hospitals & Health Networks*
- **100 Best Places to Work in Healthcare**-*Becker's Hospital Review*

2012

- **America's Best Hospitals for gastroenterology, orthopedics and pulmonology**-*U.S. News & World Report*
- **Leapfrog "A" Grade for Patient Safety**-*The Leapfrog Group*
- **Accredited Chest Pain Centers**-*Society of Cardiovascular Patient Care*
- **100 Most Wired Hospitals**-*Hospitals & Health Networks*
- **NCI Community Cancer Centers Program (NCCCP) redesignation**-*National Cancer Institute, U.S. National Institutes of Health*
- **100 Best Places to Work in Healthcare**-*Becker's Hospital Review*
- **Computerworld Honors Laureate**-*Computerworld Magazine*
- **VHA Leadership Award for Supply Chain Management Excellence**-*VHA*
- **HealthGrades Emergency Medicine Excellence Awards (LVH and LVH-Muhlenberg)**-***HealthGrades***
- **Certified Comprehensive Stroke Center**-*Joint Commission*

2013-2014

- **America's Best Hospitals in 7 specialties**-*U.S. News & World Report - 2013*
- **America's Best Hospitals in 10 specialties**-*U.S. News & World Report - 2014*
- **Magnet Prize®**-*American Nursing Credentialing Center*
- **Leapfrog "A" Grade for Patient Safety**-*The Leapfrog Group 2013 & 2014*
- **America's Safest Hospitals**-*AARP*
- **Most Wired Hospitals**-*Hospitals & Health Networks*
- **Integrated Health System to Know**-*Becker's Hospital Review*
- **100 Best Places to Work in IT**-*Computerworld Magazine*

2015-2016

- **America's Best Hospitals in 7 specialties**-*U.S. News & World Report – 2015*
- **America's Best Hospitals in 5 specialties**-*U.S. News & World Report - 2016*
- **Leapfrog "A" Grade for Patient Safety**-*The Leapfrog Group – 2015*
- **Circle of Life for Palliative Care**-*American Hospital Association*
- **Most Wired Hospitals**-*Hospitals & Health Networks Group – 2015*
- **Most Wired Advanced**-*Hospitals & Health Networks Group – 2016*
- **"Above Average" In Aortic Valve Replacement**-*Consumer Reports*
- **Re-certified Comprehensive Stroke Center**-*Joint Commission*
- **Magnet Hospital redesignation for nursing excellence**-*American Nursing Credentialing Center - 2016*

Objectives

- After this presentation, participants will be able to:
  - Define uncontrolled or refractory seizures
  - Summarize possible causes of uncontrolled seizures
  - Differentiate epilepsy versus epileptic syndromes
  - Describe epilepsy general classifications and mimics
  - Describe epilepsy investigation and treatment

Epilepsy is not a benign disease

- Epilepsy is among the most common serious neurological conditions, affecting 1 in 26 people
- Has no geographic, social, or racial boundaries
- Affects people of all ages
- Frequently associated with comorbidities not just seizures

What are “uncontrolled” or “refractory” seizures?

- Seizures are not controlled with seizure medications
  - Other terms may include: “uncontrolled,” “intractable,” “refractory,” or “drug resistant”
- Data suggest that epilepsy fails to come quickly under control with medicines in about one-third of cases
- Epilepsy specialists strive for patients to have no seizures for the best possible control

The International League Against Epilepsy (ILAE) has proposed the following definition of drug-resistant epilepsy and suggests this term to be used:

- When a person has failed to become and/or remain seizure-free with adequate trials of two seizure medications

- Seizure medications have been chosen appropriately for the person's seizure type and well-tolerated by the person

What are possible causes of uncontrolled seizures?

- Seizures in general can be uncontrolled for a number of reasons:
  - Wrong diagnosis
  - Wrong treatment
  - Lifestyle factors and/or triggers
  - Properly diagnosed seizures do not always respond to the best medical treatment

Uncontrolled Seizures: Take-home Message

- The diagnosis has to be correct
  - If seizures can be brought under control with a different treatment, then they would not be considered refractory
- Triggers and lifestyle factors have to be addressed
  - Medication therapy may work better

What are other common reasons for uncontrolled seizures?

- Inadequate doses of medicine
- Polypharmacy and toxicity
- Missing doses (poor compliance)
- Complicating factors (illness, sleep deprivation, extreme stress)
- Brain abnormalities
- Genetic causes

Epilepsy Course

- Usually starts in childhood or early adolescence but may occur at any age
  - Newborns
  - Early school age
  - Adolescents
  - Seniors

Epilepsy Course

- 5% of the population suffer a single seizure at some point in their lives
- 0.5-1% of the population have >1 seizure = epilepsy
- 70% of epilepsy cases are well-controlled with drugs
- 30% of epilepsy cases are partially resistant to drug treatments = INTRACTABLE (or pharmacoresistant) EPILEPSY

Epilepsy versus Epileptic Syndromes

- Epilepsy is not one disease!
  - No unique etiology...
- Can be a symptom of numerous disorders referred to as symptomatic epilepsy
  - trauma, tumors, inflammation, stroke, brain degeneration
- Sometimes the cause remains unclear despite careful history taking, examination and investigation
  - Especially in children!

Epilepsy Classifications

- Based on the nature of the seizures rather than the presence or absence of an underlying cause

- Seizures that begin focally (within one hemisphere) are thus distinguished from those of a generalized nature which probably begin in deeper structures and progress to both sides simultaneously

Epilepsy Classifications

- Focal seizures
  - Account for 80% of adult epilepsy
    - Simple partial seizures
    - Complex partial seizures
    - Partial seizures secondarily generalized
- Generalized seizures
  - More common in children
    - Absence seizures (Staring)
    - Myoclonic seizures (Brief jerking episodes)
    - Clonic seizures (Uncontrolled prolonged jerks)
    - Tonic seizures (Stiffening/rigid)
    - Atonic seizures (Dropping)

Focal (partial) seizures

Focal seizures evolving to generalized convulsions:
secondary generalised tonic/clonic seizures (sGTCS)

Status Epilepticus

- Consciousness does not return between seizures for more than 30 min
  - Potentially life-threatening with the development of deepening coma and circulatory collapse
  - Death occurs in 5-10% or more depending on the underlying cause

- Status epilepticus may occur with strokes (especially in elderly), following head injury, on reducing drug therapy, with alcohol withdrawal or drug intoxication, with metabolic disturbances or during pregnancy

- Treatment: intravenous seizure medications ASAP, general anesthesia with propofol or other medications should then be started

Epilepsy Mimics

- Fainting attacks—result from reduced cerebral blood flow; prodromal pallor, nausea, sweating; jerks occur commonly!
- Irregular heart rhythm
- Migraines (some forms)
- Low blood sugar (can be life-threatening)
- Sleep disorders like narcolepsy – inappropriate sudden sleep episodes
- Panic attacks
- Non-epileptic spells

Epilepsy – Investigation

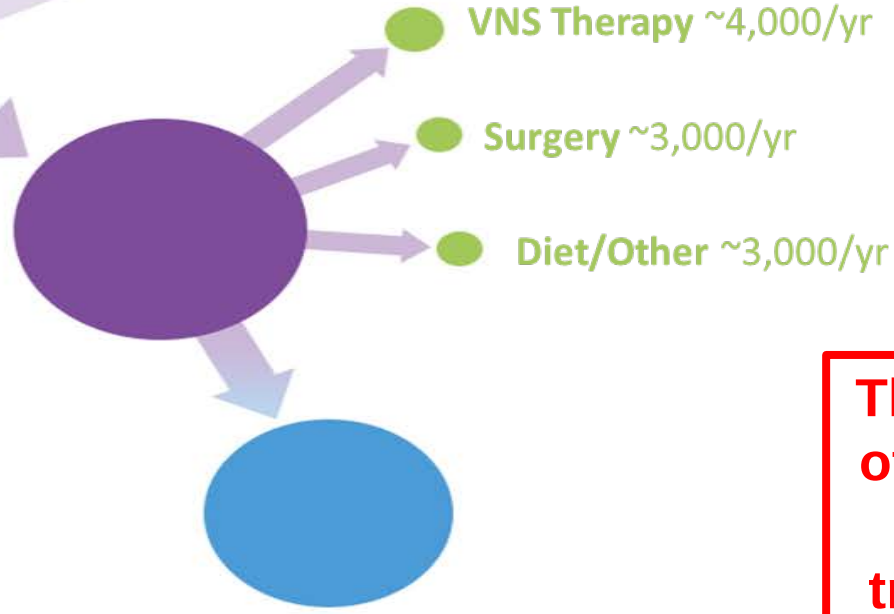
- Epilepsy may be a symptom of a treatable condition
- Routine investigation can include blood work or chest X-ray depending on the situation
- Electroencephalogram (EEG):
  - **Specialized EEG investigations:** Sleep-deprived EEG, ambulatory EEG and video-EEG monitoring
- Brain CT or (preferably) MRI performed in all persons aged 25 or more presenting with first seizure and in people with focal epilepsy irrespective of age.

Treatment Gaps for Drug-resistant Epilepsy (DRE)

- 2.9 million in US with Epilepsy
- DRE in 870,000
- DRE = Epilepsy patients failing 2+ medications

Continuing medications without evaluation ~810,000/year

Epilepsy Monitoring Unit (EMU) Stays ~60,000/yr



Evaluated but untreated ~50,000/year

Thus, only 1-2% of DRE patients receive treatment each year

VNS Therapy

Controls seizures by sending mild pulses to the left vagus nerve in the neck at regular intervals all day, every day

Short outpatient procedure, typically 1-2 hours

Indication

Approved in the US in **1997** for use as an **adjunctive** therapy in reducing the frequency of seizures

- in adults and adolescents over 12 years of age
- with partial onset seizures that are refractory to antiepileptic medications

VNS Therapy is the most established device solution for DRE

>85,000

patients treated[1]

>1,000

peer-reviewed publications on VNS Therapy

>25 years

worldwide patient experience[1]

Assessed 3 times by AAN

Evidence confirmed

VNS Therapy for epilepsy is both **effective** and **safe**[2-4]

The RNS® System

The world's only Brain-Responsive Neurostimulation System

- **The RNS System is indicated for patients who**:
- Are 18 years or older
- Have failed 2 medications
- Have partial onset seizures that are localized to 1 or 2 foci
- **Other considerations**:
- Patients at risks of neurological/cognitive deficits with resection
- Patients who choose not to have a resection
- Equally effective across variety of patients:
  - Treated and not treated with VNS
  - Treated and not treated with epilepsy surgery

Introduction to the RNS® System

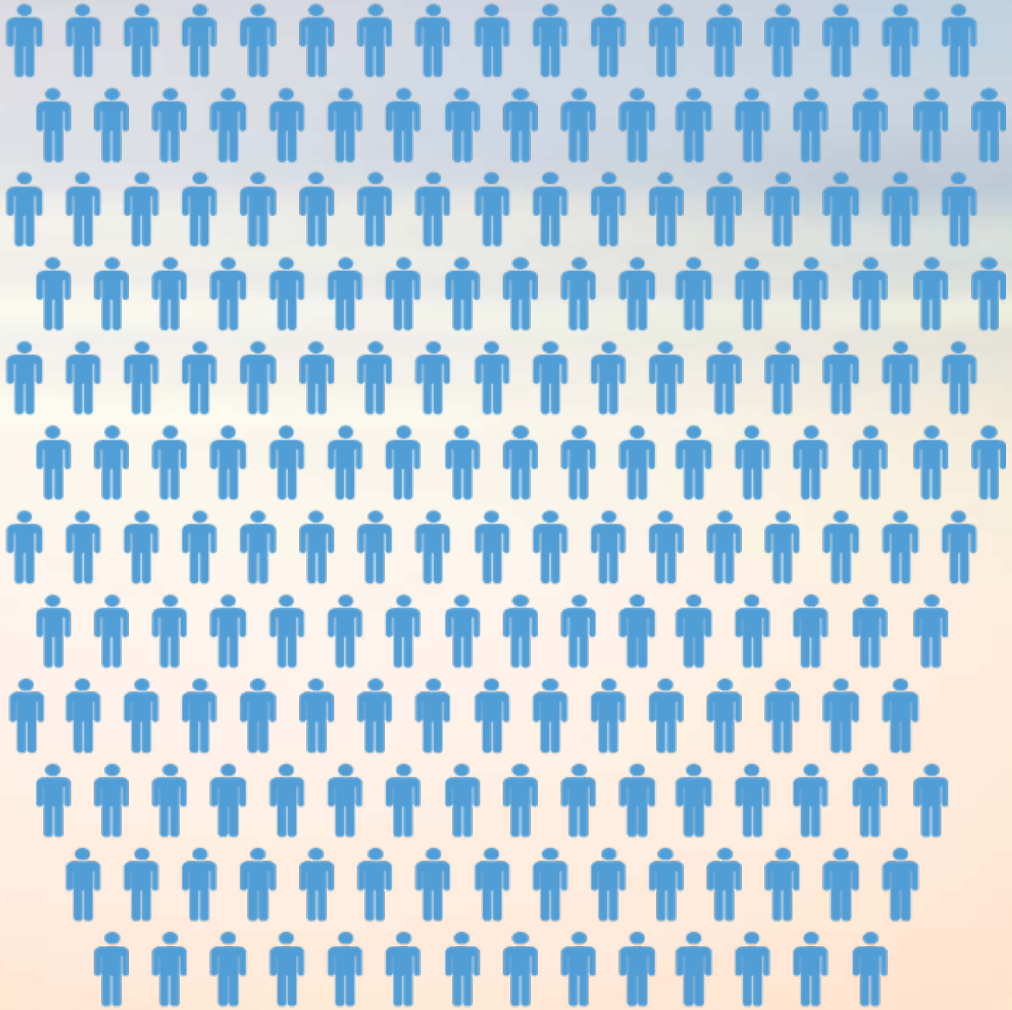
Brain-responsive neurostimulation

Who will you help tomorrow?

By the time we return to work tomorrow…

DRE patients in the US will experience nearly **200** catastrophic life events

- **77** ER visits
- **35** fractures, head traumas or status epilepticus
- **17** hospitalizations
- **51** deaths



Adapted from Helmers SL, et al. Epilepsy Behav 2011;22:370-5. Incidence per 12 hours.

Epilepsy - Treatment

- In refractory cases surgery may be necessary
  - Target is seizure-freedom and improvement in quality of life!

- Common drugs used in clinical practice
  - Carbamazepine (Tegretol)
  - Sodium valproate (Depakote)
  - Lamotrigine (Lamictal)
  - Levetiracetam (Keppra)
  - Topiramate (Topamax)
  - Pregabalin (Neurontin)
  - Zonisamide (Zonegran)

- Basic rules for drug treatment:
  - Simple regimen, preferably using one anticonvulsant (monotherapy)
  - “Start low, increase slow”
  - Add-on another medicine is necessary if seizures continue

Treatment Goals and Strategies

Newly Diagnosed Epilepsy

- No seizures
- No side effects

DRE

- Optimize long-term seizure control
- Maximize quality of life
- Minimize side effects
- Maximize adherence
- Decrease seizure severity/postictal period

Summary

- Different terms may be used to describe DRE:
  - "uncontrolled"
  - "intractable"
  - "refractory"
  - "drug resistant"
- Diagnosis must be correct and triggers/lifestyle factors addressed
- Seizures can be focal or generalized
- Beware of seizures mimics

Thank You!

Questions?

Contact Information:

Dr. Sameh Morkous
Chief of Pediatric Neurology
Lehigh Valley Health Network

Email: sameh.morkous@lvhn.org